

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (CURRENTLY AMENDED) An isolated polynucleotide comprising a nucleotide sequence chosen from:
 - a) a nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 7;
 - b) a nucleotide sequence encoding a polypeptide according to SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 or SEQ ID NO: 8, ~~wherein the polypeptide is an IGS4 polypeptide;~~
 - c) a nucleotide sequence of the DNA insert contained in the deposit no. CBS102221 or the deposit no. CBS102222 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands;
 - ~~d) a nucleotide sequence having at least 80% sequence identity over its entire length to the nucleotide sequence of (a), (b), or (c); or~~
 - [[e]] d) a nucleotide sequence which is complimentary to the nucleotide sequence of (a) or (b) or (c) [[or (d)]].
2. (CURRENTLY AMENDED) The polynucleotide of claim 1 wherein said polynucleotide comprises:
 - a) the nucleotide sequence contained in SEQ ID NO: 1 encoding the [[IGS4]] polypeptide of SEQ ID NO: 2;

b) the nucleotide sequence contained in SEQ ID NO: 3 encoding the [[IGS4]] polypeptide of SEQ ID NO: 4;

c) the nucleotide sequence contained in SEQ ID NO: 5 encoding the [[IGS4]] polypeptide of SEQ ID NO: 6; or

d) the nucleotide sequence contained in SEQ ID NO: 7 encoding the [[IGS4]] polypeptide of SEQ ID NO: 8.

3-4. (CANCELED)

5. (PREVIOUSLY PRESENTED) The isolated polynucleotide of claim 1 which is DNA or RNA.

6. (CURRENTLY AMENDED) An isolated ~~nucleotide sequence~~ polynucleotide encoding an ~~IGS4~~ a neuromedin receptor protein of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8, said protein exhibiting ~~high affinity~~ ligand binding for neuromedin U with a log EC₅₀ value of at least below -6.00.

7. (CURRENTLY AMENDED) The isolated ~~nucleotide sequence~~ polynucleotide of claim 6 encoding a polypeptide, wherein said polypeptide is expressed in at least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea.

8. (CURRENTLY AMENDED) An isolated ~~nucleotide sequence~~ polynucleotide encoding ~~an IGS4~~ a neuromedin receptor protein of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8, wherein said protein exhibits ~~high affinity~~ ligand binding for neuromedin U with a log EC₅₀ value of at least below -6.00, and is expressed in at least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea, and said nucleotide sequence being selected from the group of nucleotide sequences as defined in claim 1.

9. (CURRENTLY AMENDED) An expression system comprising a DNA or RNA molecule, wherein said expression system produces ~~[[an IGS4]]~~ a polypeptide comprising an amino acid sequence, ~~which has at least 80% identity with the~~ polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 or SEQ ID NO: 8 or with the polypeptide encoded by the DNA insert contained in the deposit no. CBS1 02221 or the deposit no. CBS1 02222 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands, when said expression system is present in a compatible host cell.

10. (CURRENTLY AMENDED) An expression system comprising an isolated DNA or RNA molecule, wherein said expression system produces ~~an IGS4~~ a polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8, which comprises ~~comprising an amino acid sequence which is~~ a neuromedin receptor protein, wherein said protein exhibits ~~high affinity~~ ligand binding for neuromedin U with a log

EC₅₀ value of at least below -6.00, and is expressed in at least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea.

11. (PREVIOUSLY PRESENTED) A host cell comprising the expression system of claim 9.

12. (PREVIOUSLY PRESENTED) The host cell according to claim 11 wherein the host cell is a yeast cell.

13. (CURRENTLY AMENDED) ~~[[A]]~~ The host cell according to claim 11 wherein the host cell is an animal cell.

14. (CURRENTLY AMENDED) A membrane preparation prepared from a cell, wherein the cell comprises an expression system comprising a DNA or RNA molecule, wherein said expression system produces ~~[[an IGS4]]~~ a polypeptide comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 or the polypeptide encoded by the DNA insert contained in the deposit no. CBS1 02221 or the deposit no. CBS1 02222 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands, when said expression system is present in a compatible host cell.

15. (CURRENTLY AMENDED) A process for producing ~~[[an IGS4]]~~ a polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8

comprising culturing the host cell of claim 11 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.

16. (CURRENTLY AMENDED) A process for producing a cell which produces ~~[[an IGS4]]~~ a polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 comprising transforming or transfecting a host cell with the expression system of claim 9 such that the host cell, under appropriate culture conditions, produces ~~an IGS4 polypeptide~~ a neuromedin receptor protein of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8.

17. (CURRENTLY AMENDED) An isolated ~~[[IGS4]]~~ polypeptide comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 or the polypeptide encoded by the DNA insert contained in the deposit no. CBS102221 or the deposit no. CBS102222 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands ~~over its entire length~~.

18. (CANCELED)

19. (CURRENTLY AMENDED) An isolated ~~[[IGS4]]~~ polypeptide of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 ~~comprising an amino acid sequence of a neuromedin receptor protein~~, wherein said polypeptide is a neuromedin receptor protein that exhibits ~~exhibiting high affinity~~ ligand binding for neuromedin U with a log EC₅₀ value of at least below -6.00.

20. (CURRENTLY AMENDED) The isolated ~~[[IGS4]]~~ polypeptide of claim 19 ~~comprising an amino acid sequence of a neuromedin receptor protein~~, wherein said neuromedin receptor protein is expressed in at least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea.

21. (CURRENTLY AMENDED) An isolated ~~[[IGS4]]~~ polypeptide ~~comprising an amino acid sequence of a neuromedin receptor protein~~, wherein said polypeptide protein exhibits high-affinity ligand binding for neuromedin U with a log EC₅₀ value of at least below -6.00, and wherein said protein is expressed in at least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea, ~~and said wherein the~~ amino acid sequence of the protein is being selected from the group of amino acid sequences as defined in claim 17.

22-25. (CANCELED)

26. (CURRENTLY AMENDED) A method for identifying agonists to ~~[[the]]~~ an isolated ~~IGS4 polypeptide~~ neuromedin receptor protein, ~~of claim 17~~ comprising:

(a) contacting a cell which produces an ~~IGS4 polypeptide~~ a neuromedin receptor protein with a test compound, wherein the neuromedin receptor protein comprises an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8

or the polypeptide encoded by the DNA insert contained in the deposit no. CBS102221
or the deposit no. CBS 102222 at the Centraalbrueau voor Schimmelcultures at Baarn
the Netherlands over its entire length; and

(b) determining whether the test compound effects a signal generated by
activation of the ~~IGS4~~ polypeptide neuromedin receptor protein in the cell.

27. (CANCELED)

28. (CURRENTLY AMENDED) A method for identifying agonists to an ~~IGS4~~
a neuromedin receptor protein, wherein said protein exhibits ~~high affinity~~ ligand binding
for neuromedin U with a log EC₅₀ value of at least below -6.00, comprising:

(a) contacting a cell which produces an ~~IGS4~~ a neuromedin receptor protein of
SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 or SEQ ID NO: 8 with a test compound;
and

(b) determining whether the test compound effects a signal generated by
activation of the [[IGS4]] neuromedin receptor protein.

29. (PREVIOUSLY PRESENTED) The method of claim 28, wherein said
agonists are effective with regard to at least one of disorders of the nervous system,
disorders of the gastrointestinal system, disorders of the cardiovascular system,
disorders of the skeletal muscle, disorders of the thyroid, lung diseases, immunological
diseases, and disorders of the genitourinary system.

30. (CANCELED)

31. (CURRENTLY AMENDED) A method for identifying antagonists to ~~[[the]]~~
~~an isolated IGS4 polypeptide~~ neuromedin receptor protein of claim 17 comprising:

(a) contacting a cell which produces ~~an IGS4 polypeptide~~ a neuromedin receptor
with an agonist, wherein the neuromedin receptor protein comprises an amino acid
sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 or the
polypeptide encoded by the DNA insert contained in the deposit no. CBS102221 or the
deposit no. CBS 102222 at the Centraalbrueau voor Schimmelcultures at Baarn the
Netherlands over its entire length; and

(b) determining whether the signal generated by said agonist in the cell is
diminished in the presence of ~~a candidate compound~~ the antagonist.

32. (CANCELED)

33. (CURRENTLY AMENDED) A method for identifying antagonists to ~~the~~
~~IGS4~~ a neuromedin receptor protein, said protein exhibiting ~~high affinity~~ ligand binding
for neuromedin U with a log EC₅₀ value of at least below -6.00, comprising:

(a) contacting a cell which produces a ~~[[IGS4]]~~ neuromedin receptor protein of
SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 with an agonist; and

(b) determining whether the signal generated by said agonist is diminished in the
presence of ~~a candidate compound~~ the antagonist.

34. (CURRENTLY AMENDED) A method for identifying antagonists to ~~the~~
~~IGS4~~ a neuromedin receptor protein according to claim 33, wherein said antagonists are
effective with regard to at least one disorder chosen from disorders of the nervous

system, the gastrointestinal system, the cardiovascular system, the skeletal muscle, the thyroid, the lung, immune system, or the genitourinary system.

35. (CANCELED)

36. (CURRENTLY AMENDED) A recombinant host cell, produced by the method of claim 16 wherein the host cell expresses ~~an IGS4 polypeptide~~ a neuromedin receptor protein.

37. (CANCELED)

38. (CURRENTLY AMENDED) A method of determining whether a substance is a potential ligand of ~~an IGS4~~ a neuromedin receptor protein comprising:

(a) contacting cells expressing ~~an IGS4 polypeptide~~ a neuromedin receptor protein of one of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6 and SEQ ID NO: 8, or contacting ~~[[the]]~~ a receptor membrane preparation of claim 14 prepared from a cell, wherein the cell comprises an expression system that produces a neuromedin receptor protein comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8 or the polypeptide encoded by the DNA insert contained in the deposit no. CBS102221 or deposit no. CBS102222 at the Centraalbureau voor Schimmelcultures at Baarn the Netherlands, when said expression system is in a compatible host cell, with labeled neuromedin U in the presence and in the absence of the substance; and

(b) measuring the binding of neuromedin U to the ~~IGS4 polypeptide~~ neuromedin receptor protein of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8.

39. (PREVIOUSLY PRESENTED) An isolated polypeptide according to claim 17, wherein the polypeptide binds neuromedin U, and has an affinity of about at least $\log EC_{50} = -6$.

40. (PREVIOUSLY PRESENTED) An isolated polypeptide according to claim 17, wherein the polypeptide binds neuromedin U, and has an affinity of at least about $\log EC_{50} = -9$.

41. (CANCELED)

42. (CURRENTLY AMENDED) The isolated polynucleotide of claim 6, wherein the [[IGS4]] neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

43. (CURRENTLY AMENDED) The isolated ~~nucleotide sequence~~ polynucleotide of claim 8, wherein the [[IGS4]] neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

44. (CURRENTLY AMENDED) The expression system ~~isolated DNA or RNA molecule~~ of claim 10, wherein the [[IGS4]] neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

45. (CURRENTLY AMENDED) The isolated ~~IGS4~~-polypeptide of claim 19, wherein the ~~[[IGS4]]~~ neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

46. (CURRENTLY AMENDED) The isolated ~~IGS4~~-polypeptide of claim 21, wherein the ~~IGS4-neuromedin-receptor protein~~ polypeptide is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

47. (CANCELED)

48. (CURRENTLY AMENDED) The method of identifying agonists of claim 28, wherein the ~~[[IGS4]]~~ neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

49. (CANCELED)

50. (CURRENTLY AMENDED) The method of identifying antagonists of claim 33, wherein the ~~[[IGS4]]~~ neuromedin receptor protein is a mammalian neuromedin receptor protein and neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

51. (CANCELED)

52. (PREVIOUSLY PRESENTED) The isolated polypeptide of claim 39, wherein the neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

53. (CURRENTLY AMENDED) The isolated polypeptide of claim 40, wherein the neuromedin U is at least one of neuromedin U-8, neuromedin U-23, and neuromedin U-25.

54. (PREVIOUSLY PRESENTED) A host cell comprising the expression system of claim 10.

55. (CURRENTLY AMENDED) The method of identifying agonists to the [[IGS4]] neuromedin receptor protein according to claim 29, wherein disorders of the nervous system are disorders of the central nervous system (CNS) or the peripheral nervous system (PNS).

56. (CURRENTLY AMENDED) The method for identifying antagonists to the [[IGS4]] neuromedin receptor protein according to claim 34, wherein disorders of the nervous system are disorders of the central nervous system (CNS) or the peripheral nervous system (PNS).

57-59. (CANCELED)

60. (CURRENTLY AMENDED) An isolated [[IGS4]] polypeptide comprising an amino acid sequence of a neuromedin receptor protein, wherein said protein exhibiting high affinity binding for neuromedin U, wherein said protein is expressed in at

least one of brain, skeletal muscle, cerebellum, testis, corpus callosum, spinal cord, substantia nigra, medulla, thalamus, caudate nucleus, pons, nucleus accumbens, fetal brain, stomach, heart, thyroid gland, lung, thymus, prostate, and trachea, and said amino acid sequence being selected from the group of amino acid sequences as defined in claim 18.

61-67. (CANCELED)

68-69. (CANCELED)